High Production Volume (HPV) Challenge Program

DIETHYLHYDROXYLAMINE
(CAS# 3710-84-7)
Test Plan

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EXECUTIVE SUMMARY

Arkema Inc has volunteered to sponsor diethylhydroxylamine (DEHA, CAS# 3710-84-7) in the USEPA HPV program. The DEHA Test Plan is being submitted to fulfill the United States Environmental Protection Agency (USEPA) High Production Volume (HPV) Challenge Program commitment for DEHA (CASN 3710-84-7).

Data from company proprietary files, peer-reviewed literature, and/or calculated endpoints using widely accepted computer modeling programs have been identified for purposes of this program. Robust summaries of the available data are provided in IUCLID format in Annex I. The following table summarizes the available data and proposed testing for DEHA:

Matrix of Available and Adequate Data on DEHA

ENDPOINT	Data Available Y/N	Testing Planned? Y/N
Physical and Chemical Data		
Melting Point	Y	N
Boiling Point	Y	N
Vapor Pressure	Y	N
Partition Coefficient	Y	N
Water Solubility	Y	N
ENVIRONMENTAL FATE		
Photodegradation	Y	N
Stability in Water (Hydrolysis)	NA	NA
Transport/Distribution	Y	N
Biodegradation	Y	N
Ecotoxicity		
Acute/Prolonged Toxicity to Fish	N	Y
Acute Toxicity to Aquatic Invertebrates (*Daphnia*)	Y	N
Acute Toxicity to Aquatic Plants (Algae)	N	Y
Toxicity		
Acute Toxicity (Oral)	Y	N
Acute Toxicity (Dermal)	Y	N
Acute Toxicity (Inhalation)	Y	N
Repeated Dose	Y	N
GeneticToxicity Gene Mutation Chromosomal aberration	Y	N
Reproductive Toxicity Developmental Toxicity	Y	N

Note: **The data used to characterize the OECD SIDS endpoints for substances in this Test Plan were identified either in company proprietary files, peer-reviewed literature, and/or calculated using widely accepted computer modelling programs. All data were evaluated for study reliability in accordance with criteria outlined by the USEPA (1999a). Only studies that**

met the reliability criteria of "1" (reliable without restrictions) or "2" (reliable with restrictions) were used. Additional data are also included in the IUCLID (International Uniform Chemical Information Dataset) attached in Annex I. A more detailed discussion of the data quality and reliability assessment process used to develop this test plan is provided in Annex II.

1.1 Physico-Chemical properties

DEHA is a colorless to light yellow flammable liquid. Physico-chemical data for DEHA were either tested or estimated using EPIWIN © (USEPA, 2000) and are provided in the following table.

Table 1. Physicochemical Data

Parameter	***Value***
Melting Point	10 ºC [1]
Boiling Point	133 ºC [1]
Vapor Pressure	5 mmHg [3]
Kow Partition Coefficient	0.43 [2]
Water Solubility	35% [3]

[1]EPIWIN v3.12 – Syspro database
[2]EPIWIN v3.12; calculated using WSKOW v1.40.
[3]Arkema technical bulletin (2004)

Conclusion

Adequate data are available to assess the physical chemical properties of DEHA. No additional studies are proposed for the HPV program.

GENERAL INFORMATION ON EXPOSURE

1.2 Production Volumes

DEHA is on EPA's high production volume list indicating it is manufactured and/or imported at greater than 1 million pounds per year according to the toxic inventory update rule (IUR).

1.2.1 Use Pattern:

The principal uses of DEHA are as free radical scavengers widely-used as a short-stopping Agent, as an oxygen scavenger for boiler water applications and as a component in photographic developing formulations.

1.3 Environmental Exposure and Fate

Environmental fate data for DEHA were either tested or estimated using EPIWIN and are provided in the following sections.

1.3.1 Photodegradation

Experimental data are reported in EPIWIN 3.12. The experimental OH rate constant for DEHA is 101 E-12 cm3/molecule. The estimated half-life of DEHA is 1.53 hours.

Conclusion

Adequate data are available to assess the photodegradation of DEHA. No additional studies are proposed for the HPV program.

1.3.2 Stability in Water

EPIWIN was unable to calculate a hydrolysis rate for DEHA.

1.3.3 Transport between Environmental Compartments

Fugacity modeling for DEHA was conducted using EPIWIN (v3.12):

Table 3. Fugacity Results for DEHA

Compartment	Mass amount (%)	Estimated half life (hr)
Air	0.283%	2.51
Water	44.9%	360
Soil	54.8%	720
Sediment	0.0842%	3.24e3

Conclusion
Adequate date are available to assess the transport of DEHA between environmental compartments. No additional studies are proposed for the HPV program.

1.3.4 Biodegradation

DEHA was not readily biodegradable when evaluated in an ISO 7827. The degradation was 17% following 28 days exposure.

Conclusion

Adequate data are available to assess the biodegradation of DEHA. No additional studies are proposed for the HPV program.

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2 HEALTH HAZARDS

2.1.1 Acute Toxicity

Acute toxicity studies via oral, dermal, and inhalation routes for DEHA have been conducted according to relevant OECD/EEC guidelines or methods comparable to those guidelines. Single exposure (acute) studies indicate that DEHA is slightly toxic if swallowed (rat LD50 2,190 mg/kg) or absorbed through skin (rabbit LD50 1,300 mg/kg), practically non-toxic if inhaled (rat 4-hr LC50 3,140 ppm), slightly irritating to rabbit eyes and slightly to moderately irritating to rabbit skin. No skin allergy was observed in guinea pigs following repeated exposure.

Conclusion

Adequate data are available to assess the acute toxicity of DEHA. No additional testing is proposed for purposes of the HPV program.

2.1.2 Repeated Dose Toxicity

DEHA was evaluated in a 28-day repeated dose study on rats according to EEC guidelines. Rats were exposed nose-only to 0, 15, 150, or 150 ppm DEHA for 6 hours per day for 28 days. Satellite groups were evaluated following a 2 week recovery period. Results from this study showed decreased body weights, food consumption, hypoactivity, changes in white blood cell counts, reduced thymus gland weight and increased liver weight. Reversible microscopic changes were noted in the nasal mucosa. The no observed adverse effect level was 150 ppm.

Conclusion

Adequate data are available to assess the repeated dose toxicity of DEHA. No additional testing is proposed for purposes of the HPV program.

2.1.3 Mutagenicity

Studies in Animals

In vitro Studies

Several reliable genetic toxicity studies are available for DEHA. Both positive and negative results were obtained with DEHA was tested in vitro (negative bacterial mutagenicity assay, positive in vitro chromosome aberration study using human lymphocytes, positive mouse lymphoma assay). Negative results were obtained when DEHA was evaluated in vivo (mouse micronucleus, unscheduled DNA synthesis).

Conclusion

Adequate data are available to assess the genetic toxicity of DEHA. No additional testing is proposed for purposes of the HPV program.

2.1.4 Developmental/Reproductive Toxicity

Reproductive Toxicity

Data from the 28 day repeated dose toxicity study could be used to assess the reproductive toxicity of DEHA. No histological lesions were noted in the prostate, seminal vesicles, testes and epididymis in males and ovaries, oviducts, uterus and vagina in females. No additional studies are proposed.

Developmental Toxicity

The developmental toxicity of DEHA was evaluated in rats according to OECD Guideline 414. DEHA was administered by oral gavage on gestation days 6 to 15. Maternal toxicity included decreased body weight and food consumption at 393 and 568 mg/kg/day. No evidence of developmental toxicity was observed at any dose level.

Conclusion

Adequate data are available to assess the reproductive and developmental toxicity of DEHA. No additional testing is proposed for purposes of the HPV program.

2.2 Initial Assessment for Human Health

Data are available for the human health toxicity endpoints. No additional studies are proposed.

3 HAZARDS TO THE ENVIRONMENT

3.1 Aquatic Effects

Acute Toxicity Test Results

DEHA is slightly toxic to daphnia. The 48 hour immobilization was calculated to be 110.5 mg/l. No data are available for acute fish and alga. An acute fish toxicity (OECD 201) and algal growth inhibition (OECD 203) are proposed for DEHA.

Conclusion

Adequate data are available to assess the toxicity to daphnia. To fulfil the fish and alga endpoints an acute fish toxicity and algal growth inhibition studies are proposed.

4 REFERENCES

Atofina, 2001. IUCLID Data Set, CAS No. 3710-, diethylhydroxylamine. Atofina, Paris, France.

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U.S. Environmental Protection Agency (USEPA), Office of Pollution Prevention and Toxics. 1998. Guidance for Meeting the SIDS Requirements: Chemical Right-to-Know Initiative.

USEPA, Office of Pollution Prevention and Toxics. 1999b. Draft Determining the Adequacy of Existing Data.

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ANNEX I: DIETHYHYDROXYLAMINE IUCLID

See attached IUCLID document.

ANNEX II: DATA QUALITY ASSESSMENT

Available environmental, ecotoxicity, and mammalian toxicity studies were reviewed and assessed for reliability according to standards specified by Klimisch et al., (1997), as recommended by the USEPA (1999a) and the OECD (OECD, 2002). The following reliability classification (Klimisch rating) has been applied to each study assessed:

- *1 = Reliable without Restriction* – Includes studies that comply with USEPA- and/or OECD-accepted testing guidelines and were conducted using Good Laboratory Practices (GLPs) and for which test parameters are complete and well documented;

- *2 = Reliable with Restriction* – Includes studies that were conducted according to national/international testing guidance and are well documented. May include studies that were conducted prior to establishment of testing standards or GLPs but meet the test parameters and data documentation of subsequent guidance; also includes studies with test parameters that are well documented and scientifically valid but vary slightly from current testing guidance. Also included in this category were physical-chemical property data obtained from reference handbooks, as well as environmental endpoint values obtained from an accepted method of estimation (e.g., USEPA's EPIWIN estimation program);

- *3 = Not Reliable* – Includes studies in which there are interferences in either the study design or results that provide scientific uncertainty or in which documentation is insufficient; and,

- *4 = Not Assignable* – This designation is used in this dossier for studies that appear scientifically valid but for which insufficient information is available to adequately judge robustness.

Those studies receiving a Klimisch rating of 1 or 2 are considered adequate to support data assessment needs in this dossier. Those key studies selected for inclusion are considered typical of the endpoint responses observed in other studies of a similar nature and design that were identified during our search of the literature.